

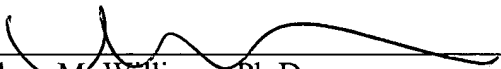
Serial No.: 09/731,261

Amendments to the specification are indicated in the attached "Marked Up Version of Amendments" (pages 9- 14).

Respectfully submitted,

Date:

5/14/02


Kathleen M. Williams, Ph.D.

Registration No.: 34,380

Customer No.: 29933

Palmer & Dodge LLP

111 Huntington Avenue

Boston, MA 02199-7613

Telephone: (617) 239-0100

MARKED-UP VERSION OF AMENDMENTS:

Specification Amendments Under 37 C.F.R. § 1.121(b)(1)(iii)

Please replace the indicated paragraphs with the following replacement paragraphs below, which are marked up by way of bracketing and underlining to show the changes relative to the previous version of the paragraph:

Please replace the paragraph at page 15 lines 21 through 22, with the following replacement paragraph:

--Figure 2 shows the result of RT-PCR performed using mRNA obtained from 50 rat islets. Forward and reverse primers are indicated. The depicted primer sequences are: forward primer GCGGGGCGGTGCGTGACTAC (SEQ ID No:) and reverse primer GGGTGGTGAGGGTTGAGGTTTGTG (seq id No: 55). The single band of 834 bp was sequenced and identified substantially as the sequence for nestin.--

Please replace the paragraph at page 16 line 3, with the following replacement paragraph:

--Figure 7 [is] depicts the nestin amino acid (SEQ ID No: 2) and nucleotide (SEQ ID No:1) sequences.--

Please replace the paragraph at pages 19 lines 17 through 28 continuing to page 20, lines 1 through 28 and page 21, lines 1 through 20, with the following replacement paragraph:

--RT-PCR and Southern blot analysis are performed according to the following methods. Total cellular RNA prepared from rat or human islets is reverse transcribed and amplified by PCR for about 35 cycles depending on the desired degree of amplification, as described previously (Daniel, et al., 1998, Endocrinology, 139:3721-3729). Oligonucleotides used as primers or amplimers for the PCR and as probes for subsequent Southern blot hybridization are:

Rat nestin: Forward, 5'gcggggcggtgcgtgactac3' (SEQ ID NO: 3);

Reverse, 5'aggcaagggggaagagaaggatgt3'(SEQ ID NO: 4);

Hybridization, 5'aagctgaagccgaatttccttgggataccagagga3' (SEQ ID NO: 5).

- Rat keratin 19: Forward, 5'acagccagtacttcaagacc3'(SEQ ID NO: 6);
Reverse, 5'ctgtgtcagcacgcacgtta3'(SEQ ID NO: 7);
Hybridization, 5'tggattccacaccaggcattgaccatgcc3' (SEQ ID NO: 8).
- Rat NCAM: Forward, 5'cagcgttgagagtcctaaat3'(SEQ ID NO: 9);
Reverse, 5'taaactcctgtggggttg3'(SEQ ID NO: 10);
Hybridization, 5'aaaccagcagcgatctcagtgggtggaacgatgat3'(SEQ ID NO: 11).
- Rat IDX-1 Forward, 5'atcactggagcaggaagt3'(SEQ ID NO: 12)
Reverse, 5'gtactacgtttcttatct3' (SEQ ID NO: 13)
Hybridization, 5'gcgtggaaaagccagtggg3'(SEQ ID NO: 14)
- Human nestin: Forward, 5'agaggggaattcctggag3'; (SEQ ID NO: 15)
Reverse, 5'ctgaggaccaggactctcta3'; (SEQ ID NO: 16)
Hybridization, 5'tatgaacgggctggagcagtctgaggaaagt3'. (SEQ ID NO: 17)
- Human keratin: Forward, 5'cttttcgcgcgccagcatt3';(SEQ ID NO: 18)
Reverse, 5'gatcttctgtccctcgagc3';(SEQ ID NO: 19)
Hybridization, 5'aaccatgaggaggaaatcagtacgctgagg3' .(SEQ ID NO: 20)
- Human glucagon: Forward, 5'atctggactccaggcgtgcc3';(SEQ ID NO: 21)
Reverse, 5'agcaatgaattccttgagc3'; (SEQ ID NO: 22)
Hybridization, 5'cacgatgaatttgagagacatgctgaagg3'; (SEQ ID NO: 23)
- Human E-Cadherin Forward, 5' agaacagcacgtacacagcc 3'(SEQ ID NO: 24)
Reverse, 5'cctccgaagaacagcaaga 3'(SEQ ID NO: 25)
Hybridization, 5' tctcccttcacagcagaactaacacacggg 3'(SEQ ID NO: 26)

Human transthyretin Forward, 5' gcagctctgccatcaatgtg 3' (SEQ ID NO: 27)

Reverse, 5' gttggctgtgaataccacct 3' (SEQ ID NO: 28)

Hybridization, 5' ctggagagctgcatgggctcacaactgagg 3' (SEQ ID NO: 29)

Human Pancreatic Amylase Forward, 5' gactttccagcagtcacctata 3' (SEQ ID NO: 30)

Reverse, 5' gtttacttctgcaggaac 3' (SEQ ID NO: 31)

Hybridization, 5' ttgcactggagaaggattacgtggcgttcta 3' (SEQ ID NO: 32)

Human procarboxypeptidase Forward, 5' tgaaggcgagaagggtgtcc 3' (SEQ ID NO: 33)

Reverse, 5' ttcgagatacaggcagatat 3' (SEQ ID NO: 34)

Hybridization, 5' agttagactttatgtctgcctgtgtctca 3' (SEQ ID NO: 35)

Human Synaptophysin Forward, 5' cttcaggtgcaccaagtgt 3' (SEQ ID NO: 36)

Reverse, 5' gttgaccatagtcaggctgg 3' (SEQ ID NO: 37)

Hybridization, 5' gtcagatgtgaagatggccacagaccaga 3' (SEQ ID NO: 38)

Human Hepatocyte Growth Factor (HGF)

Forward, 5' gcatcaaatgtcagccctgg 3' (SEQ ID NO: 39)

Reverse, 5' caacgctgacatggaattcc 3' (SEQ ID NO: 40)

Hybridization, 5' tcgaggtctcatggatcatacagaatcagg 3' (SEQ ID NO: 41)

Human cMET (HGF-receptor) Forward, 5' caatgtgagatgtctccagc 3' (SEQ ID NO: 42)

Reverse, 5' cctttagattgcaggcaga 3' (SEQ ID NO: 43)

Hybridization, 5' ggactcccatccagtgtctccagaagtgtat 3' (SEQ ID NO: 44)

Human XBP-1 Forward, 5' gagtagcagctcagactgcc 3' (SEQ ID NO: 45)

Reverse, 5' gtagacctctgggagctcct 3' (SEQ ID NO: 46)

Hybridization, 5' cgcagcactcagactacgtgcacctctgca 3' (SEQ ID NO: 47)

Human Glut-2

Forward, 5' gcagctgtcactaatcac 3' (SEQ ID NO: 48)

Reverse, 5' tcagcagcacaagtcccact 3' (SEQ ID NO: 49)

Hybridization, 5' acgggcattcttattagtcagattattggt 3' (SEQ ID NO: 50)

Human Insulin

Forward, 5' aggtcttcttacaca3' (SEQ ID NO: 51)

Reverse, 5' caggctgcctgcacca 3' (SEQ ID NO: 52)

Hybridization, 5' aggcagaggacctgca 3' (SEQ ID NO: 53).--

Please replace the paragraph at pages 46 line 28 continuing to page 47, lines 1 through 24 with the following replacement paragraph:

--Total cellular RNA prepared from rat or human islets was reverse transcribed and amplified by PCR for 35 cycles as described previously (Daniel et al., 1998, Endocrinology, 139:3721-3729). The oligonucleotides used as primers or amplimers for the PCR and as probes for subsequent Southern blot hybridization are:

Rat nestin:

Forward, 5' gcggggcggtgcgtgactac3' (SEQ ID NO: 3);

Reverse, 5' aggcaaggggaagagaaggatgt3' (SEQ ID NO: 4);

Hybridization, 5' aagctgaagccgaattccttgggataccagagga3' (SEQ ID NO: 5).

Rat keratin 19:

Forward, 5' acagccagtacttcaagacc3' (SEQ ID NO: 6);

Reverse, 5' ctgtgtcagcacgcacgtta3' (SEQ ID NO: 7);

Hybridization, 5' tggattccacaccaggcattgacctgccca3' (SEQ ID NO: 8).

Rat NCAM:

Forward, 5' cagcgttgagagtccaaat3' (SEQ ID NO: 9);

Reverse, 5' ttaaactcctgtggggttg3' (SEQ ID NO: 10);

Hybridization, 5' aaaccagcagcggtatctcagtggtgtggaacgatgat3' (SEQ ID NO: 11).

Rat IDX-1 Forward, 5'atcactggagcaggaagt3'(SEQ ID NO: 12)

Reverse, 5'gctactacgtttcttatct3' (SEQ ID NO: 13)

Hybridization, 5'gcgtggaaaagccagtggg3'(SEQ ID NO: 14)

Human nestin: Forward, 5'agagggaattccttgag3'; (SEQ ID NO: 15)

Reverse, 5'ctgaggaccaggactctcta3'; (SEQ ID NO: 16)

Hybridization, 5'tatgaacgggctggagcagtctgaggaaagt3'.(SEQ ID NO: 17)

Human keratin: Forward, 5'cttttcgcgcgccagcatt3';(SEQ ID NO: 18)

Reverse, 5'gatcttctgtccctcgagc3';(SEQ ID NO: 19)

Hybridization, 5'aaccatgaggaggaaatcagtacgctgagg3'.(SEQ ID NO: 20)

Human glucagon: Forward, 5'atctggactccaggcgtgcc3';(SEQ ID NO: 21)
Reverse, 5'agcaatgaattccttggcag3'; (SEQ ID NO: 22)

Hybridization, 5'cacgatgaatttgagagacatgctgaagg3'; (SEQ ID NO: 23).--

Please replace the paragraph on page 50, lines 16 through 24 with the following replacement paragraph:

--Insulin and glucagon concentrations in culture media were determined by ultra sensitive radioimmunoassay kits purchased from Linco Research Inc. and DPC Inc., respectively. The antisera supplied in the respective kits are guinea pig anti-human insulin and rabbit anti-human glucagon. GLP-1 secretion was measured with an anti-human GLP-1(7-36)amide rabbit polyclonal antiserum raised by immunization of a rabbit with a synthetic peptide CFIAWLVKGR (SEQ ID NO: 54) amide conjugated to keyhole limpet hemocyanin. The antiserum is highly specific for the detection of GLP-1(7-36)amide and only weakly detects proglucagon. The sensitivity levels for these assays are 6 pg/mL, 13 pg/mL and 10.2 pg/mL, respectively.--